

Remarks

Claims 32 and 34-44 and 46-55 are pending. Claims 1-33, 35-38, 45, and 51 have been canceled. Claims 34 and 47 have been amended to more clearly claim what Applicants to believe to be their invention.

Claim 34 was amended to recite “and wherein the random portion is complementary to the target sequence”. Support for amended claim 34 can be found at least on page 12, lines 23-25 where primers with a random portion complementary to a target sequence present in a nucleic acid sample of substantial complexity is described.

Claim 47 was amended to recite “wherein each primer comprises a complementary portion, wherein the complementary portions of each of the primers in the primer set are each complementary to a different portion of the hybridization target”. Support for amended claim 47 can be found at least on page 3, lines 21-23 where the same is disclosed.

Rejection Under 35 U.S.C. § 102

1. Claims 34, 39-44, 47-48, and 52-55 were rejected under 35 U.S.C. § 102(e), as being anticipated by Lupski et al. (5,691,136). Applicants respectfully traverse this rejection to the extent it applies to the claims as amended.

Lupski et al. discloses oligonucleotide primers and methods for identifying strains of bacteria by genomic fingerprinting (See Lupski et al. column 1, lines 10-20). The method described by Lupski et al. employs primers that are used to amplify bacterial genomic DNA between repetitive sequences present in the bacterial genomes. (Id.) Each primer pair disclosed within Lupski et al. is selected to be complementary to the different strands of each specific repetitive sequence (See Lupski et al. column 5, lines 15-17).

In making a rejection under 35 U.S.C. § 102, the Patent Office is burdened with establishing that the cited art teaches each and every limitation of the claims. Applicants submit that the present rejection does not meet this burden.

The passages of Lupski et al. cited in the Office Action fail to disclose a kit for amplifying a target nucleic acid sequence wherein the target sequence is a nucleic acid sample of substantial complexity, the kit comprising, in part, a set of primers wherein the set of primers

comprises primers having random nucleotide sequences, wherein each primer comprises a constant portion and a random portion, wherein the constant portion of each primer has the same nucleotide sequence and the random portion of each primer has a random nucleotide sequence, and wherein the random portion is complementary to the target sequence. The passages of Lupski et al. cited in the Office Action also fail to disclose a kit for amplifying a target nucleic acid sequence, the kit comprising, in part, a set of primers wherein the set of primers comprises a plurality of primers, wherein each primer comprises a complementary portion, wherein the complementary portions of each of the primers in the primer set are each complementary to a different portion of the hybridization target, wherein all of the primers in the set of primers are complementary to the same strand of the target sequence, and wherein the set of primers has 3 or more primers.

Claims 34, 39-44, 52 and 54

Claim 34, as well as claim 39-44, 52 and 54 that depend from Claim 34, is drawn to a kit for amplifying a target nucleic acid sequence wherein the target sequence is a nucleic acid sample of substantial complexity, the kit comprising a set of primers wherein the set of primers comprises primers having random nucleotide sequences, and a strand displacing DNA polymerase or a DNA polymerase and strand displacement factor compatible with the DNA polymerase, wherein each primer comprises a constant portion and a random portion, wherein the constant portion of each primer has the same nucleotide sequence and the random portion of each primer has a random nucleotide sequence. As such, the claims require the set of primers to have specific attributes and abilities. In particular, the claims require: (1) a set of primers, wherein the set of primers comprises primers having random nucleotide sequences, wherein each primer comprises a constant portion and a random portion, (see claim 34, lines 3-6) wherein the constant portion of each primer has the same nucleotide sequence and the random portion of each primer has a random nucleotide sequence (see claim 47, lines 6-8) and (2) wherein the random portion is complementary to the target sequence. It is important to note that each of the primers in the primer set of the kit must contain all the attributes listed above. In other words, the random portion of the primers of the kit are the portions that are complementary to the target sequence.

This is evident throughout the application where primers for whole genome amplification are described. For example, on page 12, lines 17-27, the specification provides that the specific nucleic acid sequences present in a sample need not be known and the primers need not be designed to be complementary to any particular sequence. The key here is that the primers “need not be designed” to be complementary to any particular sequence, not that the primers are not complementary to a particular sequence. What this means is that the primers can be randomly synthesized, however they are still complementary to the target sequence. This is of particular usefulness where the target is of substantial complexity and the sequence of the target is unknown.

The Office Action alleges (page 2, lines 8-10) that each primer pair of Lupski et al. is selected to be substantially complementary to the different strands of each repetitive sequence. This allegation highlights the error of the allegation that Lupski et al. discloses the claimed kits. As described above, the random portion of the claimed primers are not specifically designed to be complementary to any particular sequence, yet they are still complementary to the target. This is different than Lupski et al. where, as admitted in the Office Action and described throughout Lupski et al., each primer pair of Lupski et al. is specifically designed to be substantially complementary to the target (repetitive sequence). In other words, the design of the primers of Lupski et al. are carried out specifically with the target sequence in mind, thus the primers are specifically designed to be complementary to a particular sequence

Furthermore, the Office Action admits (page 2, lines 16-17) that Lupski et al does not explicitly disclose that each primer has a constant portion and a random portion. The Office Action however alleges (page 2, line 20 – page 3, line 1) that the teachings of Lupski et al. are inherent that each primer has a constant portion and a random portion and the constant portion of each primer are the same. For support, the Office Action cites Figures 2 and 3 of Lupski et al. that shows the alignment of ERIC oligonucleotide primer sequences with respect to the central inverted repeat of a REP or an ERIC consensus sequence. In both Figures 2 and 3 of Lupski et al. the primers are specifically provided to be complementary to their respective target. It is the specific sequenced portions of the primers of Figures 2 and 3 responsible for hybridizing to the target. Even though the primers have an “N” sequence within the primer, this is not a random

portion complementary to the target as claimed. The “N” position is simply a possible “Wobble” base in the primer that is actually not going to be complementary to the target. If the “N” of the primers of Lupski et al. were designed to be complementary to the target, they would not be random as defined in the instant specification. Furthermore, if the “N” of the primers of Lupski et al. were designed to be complementary to the target the primer would be a completely non-random primer. Such a primer certainly does not anticipate the claim 34 and the claims dependent therefrom.

As such, the cited passage of Lupski et al. fails to disclose a kit for amplifying a target nucleic acid sequence wherein the target sequence is a nucleic acid sample of substantial complexity, the kit comprising, in part, a set of primers wherein the set of primers comprises primers having random nucleotide sequences, wherein each primer comprises a constant portion and a random portion, and wherein the random portion is complementary to the target sequence. Because Lupski et al. fails to disclose every feature of the claimed kits, Lupski et al. fails to anticipate claims. Because Lupski et al. fails to disclose every element of the claims, Applicants respectfully request withdrawal of the rejection.

Claims 47, 48, 53 and 55

Claim 47, as well as claims 48, 53 and 55 that depends from Claim 47, is drawn to a kit for amplifying a target nucleic acid sequence, comprising, in part, a set of primers wherein the set of primers comprises a plurality of primers, wherein each primer comprises a complementary portion, wherein the complementary portions of each of the primers in the primer set are each complementary to a different portion of the hybridization target, wherein all of the primers in the set of primers are complementary to the same strand of the target sequence, wherein the set of primers has 3 or more primers. As such, the claims require the set of primers to have specific attributes and abilities. In particular, the claims require: (1) that the each primer comprises a complementary portion, wherein the complementary portions of each of the primers in the primer set are each complementary to a different portion of the hybridization target (see claim 47, lines 2-4) and (2) that all of the primers in the set of primers are complementary to the same strand of the target sequence (see claim 47, lines 4-5). It is important to note that each of the primers in

the primer set of the kit must contain all the attributes listed above as well as the ability to interact with the hybridization target also described above.

The Office Action alleges (page 4, lines 7-18) that the teachings of Lupski et al. anticipate the limitations of the claims. For support, the Office Action cites sections of Lupski et al. that describe methods of identifying strains of bacteria by genomic fingerprinting as well as specific sections directed to primers that can be used in the disclosed method. Specifically, the Office Action alleges that Lupski et al. discloses that a variety of primers can be used to detect repetitive sequences in bacteria and that a plurality of primers can be added to the method where each of the primers will bind to a different sequence (see Office Action page 4, lines 9-13). It is important to note that throughout Lupski et al. methods employ pairs of primers for the detection reactions. In fact, the specific portion of Lupski et al. cited by the Office Action for disclosing a variety of primers can be used to detect repetitive sequences in bacteria and that a plurality of primers can be added to the method where each of the primers will bind to a different sequence specifically recites:

“In addition to the above described methods a plurality of *pairs of primers* can be added to the method. Each *pair of primers* will bind to a different repetitive sequence.” (*Emphasis ours*)

In other words, the only time multiple primers are disclosed to binding to different targets is in the context of primer pairs (See Lupski et al., column 8, line 65 – column 9, line 2) or where the primers of the primer pairs overlap the same hybridization target (See Lupski et al. Figures 2 and 3). The failure of Lupski et al. to disclose the currently claimed kits is supported in Figures 2 and 3 of Lupski et al (also cited by the Office Action), where primer pairs are described and illustrated. Each primer pair disclosed within Lupski et al. is selected to be complementary and overlapping to the different strands of each specific repetitive sequence (See Lupski et al. column 5, lines 15-17). The primers described in Figure 3, as representative of the primers taught by Lupski et al. fall into two categories, those that bind the consensus/target sequence (sense) and those that bind the complement of the consensus/target sequence (antisense). Although the sense and antisense primers bind to different regions of the consensus/target sequence, they bind to different strands of the consensus/target sequence. However, each primer in the sense or

antisense set, for example the ERIC1 and ERIC2 primers described above, bind to the same portion (overlap) of the consensus/target sequence on the particular strand of the target sequence. In other words, each primer in the primer set are NOT complementary to NOR non-overlapping of a different portion of the hybridization target. The same is true for the primers disclosed in Figure 2 for the REP sequence.

As provided above, Claim 47 is drawn to a kit that comprises, in part, a set of primers wherein the set of primers comprises a plurality of primers, wherein each primer comprises a complementary portion, wherein the complementary portions of the primers are each complementary to a different portion of the hybridization target (see claim 47, line 3-5) and wherein all of the primers in the set of primers are complementary to the same strand of the target sequence (see claim 47, lines 4-5). In other words, each of the primers in the primer set each hybridize to a different portion of the hybridization target on the same strand. In the interest of being complete, Applicants note that “the same strand of the target sequence” does not include the complementary strand of the target sequence. This is supported at least on page 34, lines 25-31 of the application, where one of the amplification methods using a set of primers where all of the primers are complementary to the same strand of the target sequence is described. Specifically, it is provided that when a set of primers where all of the primers are complementary to the same strand of the target sequence are used, only one of the strands of the target sequence is replicated. This is due to the fact that the primers do not hybridize to the complementary strand. One of skill in the art would understand this to mean that the primers of the primer set only bind one of the strands, not both strands. Lupski et al. simply does not disclose such a limitation.

Specifically, Lupski et al. fails to disclose a kit for amplifying a target nucleic acid sequence, comprising, in part, a set of primers wherein the set of primers comprises a plurality of primers, wherein each primer comprises a complementary portion, wherein the complementary portions of each of the primers in the primer set are each complementary to a different portion of the hybridization target, wherein all of the primers in the set of primers are complementary to the same strand of the target sequence, wherein the set of primers has 3 or more primers. Because

Lupski et al. fails to disclose every feature of the claimed kits, Lupski et al. fails to anticipate claims 47-48, 53 and 55. As such, Applicants respectfully request withdrawal of the rejection.

Rejection Under 35 U.S.C. § 103

1. Claims 32, 35-37, 49 and 51 were rejected under 35 U.S.C. § 103(a), as being unpatentable over Lupski et al. (5,691,136). Applicants respectfully traverse this rejection to the extent it applies to the claims as amended.

Applicants note that claim 32, 35-37 and 51 have been canceled. As such, Applicants submit that the rejection of these claims is moot.

In order for a reference or a combination of references to anticipate a claim or claims, “[f]irst, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.” MPEP § 2143.

With regard to the subject matter of Claim 49, Applicants first note that Claim 49 depends from Claim 47 and by definition encompass all the elements of Claim 47. As provided above, Claim 47 drawn to a kit for amplifying a target nucleic acid sequence, comprising, in part, a set of primers wherein the set of primers comprises a plurality of primers, wherein each primer comprises a complementary portion, wherein the complementary portions of each of the primers in the primer set are each complementary to a different portion of the hybridization target, wherein all of the primers in the set of primers are complementary to the same strand of the target sequence, wherein the set of primers has 3 or more primers. As such, the claims require the set of primers to have specific attributes and abilities. In particular, the claims require: (1) that the each primer comprises a complementary portion, wherein the complementary portions of each of the primers in the primer set are each complementary to a different portion of the hybridization target (see claim 47, lines 2-4) and (2) that all of the primers in the set of primers are complementary to the same strand of the target sequence (see claim 47, lines 4-5). It is important

to note that each of the primers in the primer set of the kit must contain all the attributes listed above as well as the ability to interact with the hybridization target also described above.

The Office Action relies on Lupski et al. in the same way and for the same disclosure for which Lupski et al. was applied in the 35 U.S.C. §102(e) rejection of claims 47, 48, 53 and 55. As discussed above in connection with the rejection under 35 U.S.C. § 102(e), Lupski et al. fails to disclose a kit for amplifying a target nucleic acid sequence, comprising, in part, a set of primers wherein the set of primers comprises a plurality of primers, wherein each primer comprises a complementary portion, wherein the complementary portions of each of the primers in the primer set are each complementary to a different portion of the hybridization target, wherein all of the primers in the set of primers are complementary to the same strand of the target sequence, wherein the set of primers has 3 or more primers. Claim 49 adds the limitation of wherein the set of primers has 5 or more primers.

As such, claims 47 and 49 require the set of primers to have specific attributes and abilities. In particular, the claims require: (1) that the each primer comprises a complementary portion, wherein the complementary portions of each of the primers in the primer set are each complementary to a different portion of the hybridization target (see claim 47, lines 2-4) and (2) that all of the primers in the set of primers are complementary to the same strand of the target sequence (see claim 47, lines 4-5). It is important to note that each of the primers in the primer set of the kit must contain all the attributes listed above as well as the ability to interact with the hybridization target also described above.

The Office Action alleges (page 4, lines 7-18) that the teachings of Lupski et al. anticipate the limitations of the claims. For support, the Office Action cites sections of Lupski et al. that describe methods of identifying strains of bacteria by genomic fingerprinting as well as specific sections directed to primers that can be used in the disclosed method. Specifically, the Office Action alleges that Lupski et al. discloses that a variety of primers can be used to detect repetitive sequences in bacteria and that a plurality of primers can be added to the method where each of the primers will bind to a different sequence (see Office Action page 4, lines 9-13). It is important to note that throughout Lupski et al. methods employ pairs of primers for the detection reactions. In fact, the specific portion of Lupski et al. cited by the Office Action for disclosing a

variety of primers can be used to detect repetitive sequences in bacteria and that a plurality of primers can be added to the method where each of the primers will bind to a different sequence specifically recites:

“In addition to the above described methods a plurality of *pairs of primers* can be added to the method. Each *pair of primers* will bind to a different repetitive sequence.” (*Emphasis ours*)

In other words, the only time multiple primers are disclosed to binding to different targets is in the context of primer pairs (See Lupski et al., column 8, line 65 – column 9, line 2) or where the primers of the primer pairs overlap the same hybridization target (See Lupski et al. Figures 2 and 3). The failure of Lupski et al. to disclose the currently claimed kits is supported in Figures 2 and 3 of Lupski et al (also cited by the Office Action), where primer pairs are described and illustrated. Each primer pair disclosed within Lupski et al. is selected to be complementary and overlapping to the different strands of each specific repetitive sequence (See Lupski et al. column 5, lines 15-17). The primers described in Figure 3, as representative of the primers taught by Lupski et al. fall into two categories, those that bind the consensus/target sequence (sense) and those that bind the complement of the consensus/target sequence (antisense). Although the sense and antisense primers bind to different regions of the consensus/target sequence, they bind to different strands of the consensus/target sequence. However, each primer in the sense or antisense set, for example the ERIC1 and ERIC2 primers described above, bind to the same portion (overlap) of the consensus/target sequence on the particular strand of the target sequence. In other words, each primer in the primer set are NOT complementary to NOR non-overlapping of a different portion of the hybridization target. The same is true for the primers disclosed in Figure 2 for the REP sequence.

As provided above, Claim 47 is drawn to a kit that comprises, in part, a set of primers wherein the set of primers comprises a plurality of primers, wherein each primer comprises a complementary portion, wherein the complementary portions of the primers are each complementary to a different portion of the hybridization target (see claim 47, line 3-5) and wherein all of the primers in the set of primers are complementary to the same strand of the target sequence (see claim 47, lines 4-5). In other words, each of the primers in the primer set each

hybridize to a different portion of the hybridization target on the same strand. In the interest of being complete, Applicants note that “the same strand of the target sequence” does not include the complementary strand of the target sequence. This is supported at least on page 34, lines 25-31 of the application, where one of the amplification methods using a set of primers where all of the primers are complementary to the same strand of the target sequence is described.

Specifically, it is provided that when a set of primers where all of the primers are complementary to the same strand of the target sequence are used, only one of the strands of the target sequence is replicated. This is due to the fact that the primers do not hybridize to the complementary strand. One of skill in the art would understand this to mean that the primers of the primer set only bind one of the strands, not both strands. Lupski et al. simply does not disclose or suggest such a limitation.

Specifically, Lupski et al. fails to disclose or suggest a kit for amplifying a target nucleic acid sequence, comprising, in part, a set of primers wherein the set of primers comprises a plurality of primers, wherein each primer comprises a complementary portion, wherein the complementary portions of each of the primers in the primer set are each complementary to a different portion of the hybridization target, wherein all of the primers in the set of primers are complementary to the same strand of the target sequence, wherein the set of primers has 3 or more primers. Because Lupski et al. fails to disclose or suggest every feature of the claimed kits, Lupski et al. fails to make obvious claim 49. As such, Applicants respectfully request withdrawal of the rejection.

2. Claims 38, 46 and 50 were rejected under 35 U.S.C. § 103(a), as being unpatentable over Lupski et al. (5,691,136) as applied to claims 32, 34-37, 39-44 and 47-49 further in view of Blanco et al. (Journal of Biological Chemistry, 1989, Vol.264(15), pg. 8935-40). Applicants respectfully traverse this rejection to the extent it applies to the claims as amended.

In order for a reference or a combination of references to anticipate a claim or claims, “[f]irst, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally,

the prior art reference (or references when combined) must teach or suggest all the claim limitations.” MPEP § 2143.

Lupski et al. discloses oligonucleotide primers and methods for identifying strains of bacteria by genomic fingerprinting (See Lupski et al. column 1, lines 10-20). The method described by Lupski et al. employs primers that are used to amplify bacterial genomic DNA between repetitive sequences present in the bacterial genomes. (Id.) Each primer pair disclosed within Lupski et al. is selected to be complementary to the different strands of each specific repetitive sequence (See Lupski et al. column 5, lines 15-17).

Claim 38 that depends from Claim 32, Claim 46 that depends from Claim 34, and Claim 50 that depends from Claim 47, all refer to the polymerase of the respective kits. Specifically, each of the claims are drawn to Φ 29 DNA polymerase. Aside from the specific enumeration of a DNA polymerase, Claims 38, 46, and 50 comprise all the limitations of the claims from which they depend.

Claim 38

With regard to the subject matter of Claim 38, Applicants note that Claim 38 has been canceled. As such, Applicants submit that the rejection of these claims is moot.

Claim 46

With regard to the subject matter of Claim 46, Applicants first note that Claim 46 depends from Claim 34 and by definition encompass all the elements of Claim 34. As provided above, Claim 34 is drawn to a kit for amplifying a target nucleic acid sequence wherein the target sequence is a nucleic acid sample of substantial complexity, the kit comprising a set of primers wherein the set of primers comprises primers having random nucleotide sequences, and a strand displacing DNA polymerase or a DNA polymerase and strand displacement factor compatible with the DNA polymerase, wherein each primer comprises a constant portion and a random portion, wherein the constant portion of each primer has the same nucleotide sequence and the random portion of each primer has a random nucleotide sequence. As such, the claims require the set of primers to have specific attributes and abilities. In particular, the claims require: (1) a set

of primers, wherein the set of primers comprises primers having random nucleotide sequences, wherein each primer comprises a constant portion and a random portion, (see claim 34, lines 3-6) wherein the constant portion of each primer has the same nucleotide sequence and the random portion of each primer has a random nucleotide sequence (see claim 47, lines 6-8) and (2) wherein the random portion is complementary to the target sequence. It is important to note that each of the primers in the primer set of the kit must contain all the attributes listed above. In other words, the random portion of the primers of the kit are the portions that are complementary to the target sequence. This is evident throughout the application where primers for whole genome amplification are described. For example, on page 12, lines 17-27, the specification provides that the specific nucleic acid sequences present in a sample need not be known and the primers need not be designed to be complementary to any particular sequence. The key here is that the primers “need not be designed” to be complementary to any particular sequence, not that the primers are not complementary to a particular sequence. What this means is that the primers can be randomly synthesized, however they are still complementary to the target sequence. This is of particular usefulness where the target is of substantial complexity and the sequence of the target is unknown.

The Office Action relies on Lupski et al. in the same way and for the same disclosure for which Lupski et al. was applied in the 35 U.S.C. §102(e) rejection of claims 34, 39-44, 52 and 54. The Office Action further admits that Lupski et al. fails to specifically disclose a kit containing phage vphi 29 DNA polymerase for strand displacement activity (See Office Action page 8, lines 3-4).

Blanco et al. which was cited for disclosing that phage vphi 29 polymerase for strand displacement fails to supplement the elements missing from Lupski et al. As discussed above in connection with the rejection under 35 U.S.C. § 102(e), Lupski et al. fails to disclose or suggest a kit for amplifying a target nucleic acid sequence wherein the target sequence is a nucleic acid sample of substantial complexity, the kit comprising, in part, a set of primers wherein the set of primers comprises primers having random nucleotide sequences, wherein each primer comprises a constant portion and a random portion, and wherein the random portion is complementary to the target sequence.

Thus, Lupski et al. and Blanco et al., either alone or in combination, fail to disclose or suggest each and every element of claim 46. Accordingly, Lupski et al. and Blanco et al. do not make obvious claim 46. Applicants respectfully request withdrawal of this rejection.

Claim 50

With regard to the subject matter of Claim 50, Applicants first note that Claim 50 depends from Claim 47 and by definition encompass all the elements of Claim 47. As provided above, Claim 47 drawn to a kit for amplifying a target nucleic acid sequence, comprising, in part, a set of primers wherein the set of primers comprises a plurality of primers, wherein each primer comprises a complementary portion, wherein the complementary portions of each of the primers in the primer set are each complementary to a different portion of the hybridization target, wherein all of the primers in the set of primers are complementary to the same strand of the target sequence, wherein the set of primers has 3 or more primers. As such, the claims require the set of primers to have specific attributes and abilities. In particular, the claims require: (1) that the each primer comprises a complementary portion, wherein the complementary portions of each of the primers in the primer set are each complementary to a different portion of the hybridization target (see claim 47, lines 2-4) and (2) that all of the primers in the set of primers are complementary to the same strand of the target sequence (see claim 47, lines 4-5). It is important to note that each of the primers in the primer set of the kit must contain all the attributes listed above as well as the ability to interact with the hybridization target also described above.

The Office Action relies on Lupski et al. in the same way and for the same disclosure for which Lupski et al. was applied in the 35 U.S.C. §102(e) rejection of claims 47, 48, 53 and 55. The Office Action further admits that Lupski et al. fails to specifically disclose a kit containing phage vphi 29 DNA polymerase for strand displacement activity (See Office Action page 8, lines 3-4). Blanco et al. which was cited for disclosing that phage vphi 29 polymerase for strand displacement fails to supplement the elements missing from Lupski et al.

As discussed above in connection with the rejection under 35 U.S.C. § 102(e), Lupski et al. fails to disclose a kit for amplifying a target nucleic acid sequence, comprising, in part, a set of primers wherein the set of primers comprises a plurality of primers, wherein each primer

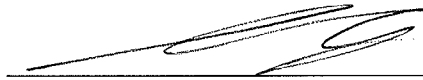
comprises a complementary portion, wherein the complementary portions of each of the primers in the primer set are each complementary to a different portion of the hybridization target, wherein all of the primers in the set of primers are complementary to the same strand of the target sequence, wherein the set of primers has 3 or more primers.

Thus, Lupski et al. and Blanco et al., either alone or in combination, fail to disclose or suggest each and every element of claim 50. Accordingly, Lupski et al. and Blanco et al. do not make obvious claim 50. Applicants respectfully request withdrawal of this rejection.

A Credit Card payment in the amount of \$230.00, representing \$230.00 for the extension of time fee for a small entity under 37 C.F.R. § 1.17(a)(2) and a Request for Two Month Extension of Time are also enclosed. This amount is believed to be correct; however, the Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 14-0629.

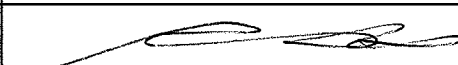
Respectfully submitted,

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